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Ambient Water Quality Criteria for Phenol

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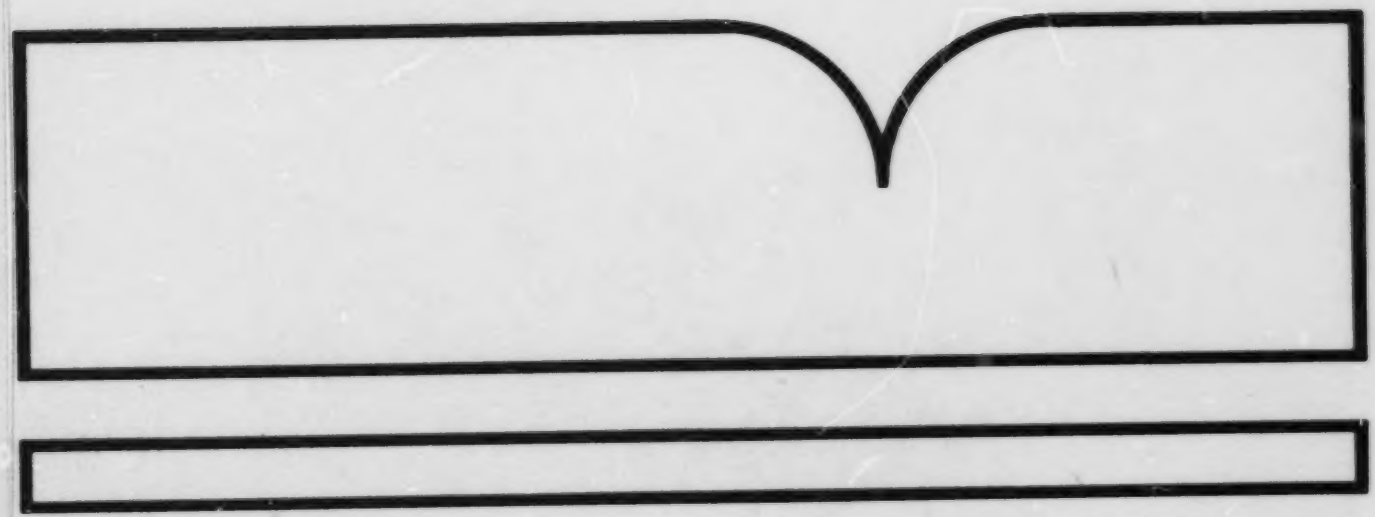

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16. ABSTRACT

Section 304(A) of the Clean Water Act [33 U.S.C. 1314(A)], requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for Phenol. It presents concentration criteria for the protection of freshwater and saltwater aquatic life. It presents 'safe' concentrations for humans, and in the case of suspect or proven carcinogens, gives various levels of incremental cancer risk. A Section 304(A) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility nor is it a water quality standard and in itself has no regulatory effect.

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AMBIENT WATER QUALITY CRITERIA FOR

PHENOL

Prepared By
U.S. ENVIRONMENTAL PROTECTION AGENCY

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FOREWORD

Section 304 (a)(1) of the Clean Water Act of 1977 (P.L. 95-217), requires the Administrator of the Environmental Protection Agency to publish criteria for water quality accurately reflecting the latest scientific knowledge on the kind and extent of all identifiable effects on health and welfare which may be expected from the presence of pollutants in any body of water, including ground water. Proposed water quality criteria for the 65 toxic pollutants listed under section 307 (a)(1) of the Clean Water Act were developed and a notice of their availability was published for public comment on March 15, 1979 (44 FR 15926), July 25, 1979 (44 FR 43660), and October 1, 1979 (44 FR 56628). This document is a revision of those proposed criteria based upon a consideration of comments received from other Federal Agencies, State agencies, special interest groups, and individual scientists. The criteria contained in this document replace any previously published EPA criteria for the 65 pollutants. This criterion document is also published in satisifaction of paragraph 11 of the Settlement Agreement in Natural Resources Defense Council, et. al. vs. Train, 8 ERC 2120 (D.D.C. 1976), modified, 12 ERC 1833 (D.D.C. 1979).

The term "water quality criteria" is used in two sections of the Clean Water Act, section 304 (a)(1) and section 303 (c)(2). The term has a different program impact in each section. In section 304, the term represents a non-regulatory, scientific assessment of ecological effects. The criteria presented in this publication are such scientific assessments. Such water quality criteria associated with specific stream uses when adopted as State water quality standards under section 303 become enforceable maximum acceptable levels of a pollutant in ambient waters. The water quality criteria adopted in the State water quality standards could have the same numerical limits as the criteria developed under section 304. However, in many situations States may want to adjust water quality criteria developed under section 304 to reflect local environmental conditions and human exposure patterns before incorporation into water quality standards. It is not until their adoption as part of the State water quality standards that the criteria become regulatory.

Guidelines to assist the States in the modification of criteria presented in this document, in the development of water quality standards, and in other water-related programs of this Agency, are being developed by EPA.

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CRITERIA DOCUMENT

PHENOL

CRITERIA

Aquatic Life

The available data for phenol indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 10,200 and 2,560 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for phenol indicate that toxicity to saltwater aquatic life occurs at concentrations as low as 5,800 µg/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of phenol to sensitive saltwater aquatic life.

Human Health

For comparison purposes, two approaches were used to derive criterion levels for phenol. Based on available toxicity data, for the protection of public health, the derived level is 3.5 mg/l. Using available organoleptic data, for controlling undesirable taste and odor qualities of ambient water, the estimated level is 0.3 mg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criterion have limitations and have no demonstrated relationship to potential adverse human health effects.

INTRODUCTION

Phenol is a large volume industrial chemical produced almost entirely as an intermediate for the preparation of other chemicals. These include synthetic polymers such as phenolic resins, bisphenol and caprolactam plastics intermediates, and chlorinated and alkylated phenols.

Phenol, occasionally referred to as "carbolic acid", is a monohydroxybenzene which is a clear, colorless (light pink when impurities are present), hygroscopic, deliquescent, crystalline solid at 25°C (Manufacturing Chemist Assoc., 1964; Kirk and Othmer, 1963; Weast, 1974). It has the empirical formula C_6H_6O, a molecular weight of 94.11, a specific gravity of 1.071 at 25°C, and a vapor pressure of 0.3513 mm Hg at 25°C (Patty, 1963; Manufacturing Chemists Assoc., 1964; Am. Ind. Hyg. Assoc., 1957; Sax, 1975). Phenol has a melting point of 43°C and a boiling point of 182°C at 760 mm Hg (Weast, 1974).

Phenol has a water solubility of 6.7 g/100 ml at 16°C and is soluble at all proportions in water at 66°C. It is also soluble in relatively non-polar solvents such as benzene, petrolatum, and oils (Patty, 1963; Kirk and Othmer, 1963; Weast, 1974).

Due to the electronegative character of the phenyl group, phenol exhibits weakly acidic properties. It possesses a pKa of 9.9 to 10.0 and readily reacts with strong bases such as NaOH, KOH, etc., to form salts called phenoxides (Weast, 1974; Kirk and Othmer, 1963). Phenoxides exist in highly alkaline aqueous solutions and many, particularly the sodium and potassium salts, are readily soluble in water.

Natural phenol is produced by the distillation of coal tar, although this source constitutes only 1 to 2 percent of total phenol production (Kirk and Othmer, 1963). The cumene process represents the most popular route of phenol production and involves two basic steps. Cumene is oxidized to cumene hydroperoxide with air in the presence of an alkali catalyst and is subsequently cleaved to phenol and acetone with the aid of a sulfuric acid catalyst (Cook, 1977). Other methods of commercial production include the toluene oxidation process and the benzene sulfonation process (Faith, et al. 1975). In the former process, toluene is oxidized to benzoic acid and reduced to phenol, using a copper catalyst. The latter method involves the sulfonation of benzene to benzenesulfonic acid, its neutralization with sodium sulfite or carbonate to form sodium benzenesulfonate and the subsequent reaction of this compound with fused caustic soda at high temperatures. The sodium phenate or sodium salt is then acidified with sulfur dioxide to form the phenol (Faith, et al. 1975). This purity of most synthetic phenols is greater than 99.5 percent, while the purity of natural sources ranges from 80 to 82 percent and 90 to 92 percent, depending upon the source and method of production. The commercial products generally contain an impurity which changes the melting point (Spector, 1956; Stecher, 1968).

Phenol or phenolic wastes also are produced during the coking of coal, distillation of wood, operation of gas works and oil refineries, manufacture of livestock dips, as a normal constitutent of human and animal wastes, and microbiological decomposition of organic matter (Bulick, 1950; Mischonsniky, 1934).

Phenol undergoes oxidation to a variety of products, such as the benzenediols, benzenetriols, and derivatives of diphenyl and diphenylene oxide, depending on the oxidizing agent and conditions (Kirk and Othmer, 1963). However, phenol may be biochemically hydroxylated to ortho- and paradihydroxybenzenes and readily oxidized to the corresponding benzoquinones. These may in turn react with numerous components of industrial waters or sewage such as mercaptans, amines, or the -SH or -NH groups of proteins. In the absence of these compounds, the quinones, especially the ortho- isomers, can be quickly destroyed by hydrolytic oxidizing reactions (Stom, 1975).

The hydroxyl group of phenol imparts a high degree of reactivity to the phenyl ring, particularly the ortho- and para- positions. Phenol has been shown to be highly reactive to chlorine in dilute aqueous solutions over a wide pH range (Carlson and Caple, 1975; Middaugh and Davis, 1976). The chlorination of phenol in aqueous solutions to form 2-chloro-, 4-chloro-, or higher chlorophenols has been demonstrated under conditions similar to those used for disinfection of wastewater effluents (Aly, 1968; Barnhart and Campbell, 1972) and represents a potential amplification of the organoleptic problems associated with phenol contamination. Synthesis of 2-chlorophenol within one hour in aqueous solutions containing as little as 10 mg/l phenol and 20 mg/l chlorine has been reported (Barnhart and Campbell, 1972). Other studies have reported the formation of up to 1.7 µg/l 2-chlorophenol and other chlorinated compounds during the chlorination or sewage effluents and power plant cooling waters (Jolley, 1973; Jolley, et al. 1975).

The photooxidation of phenol in water at alkaline pH has been studied. Irradiation with a mercury arc lamp produced several intermediate compounds and p-benzosemiquinone as the final product (Tomkiewicz, et al. 1971; Cocivera, et al. 1972). Audureau, et al. (1976) studied the photooxidation of phenol with ultraviolet irradiation (253.7 nm) and concluded that the reaction initially leads to the formation of a complex mixture of tri-and tetrahydroxybiphenyls, quinones and dihydroxybenzenes. Aqueous phenol solutions irradiated with sunlight for seven days were reported to degrade to hydroquinone and pyrocatechol (Perel'shtein and Kaplin, 1968). Subsequent irradiation of pyrocatechol with sunlight for seven days yielded pyrogallol. The end products of photodecomposition were reported to be humic acids. Conversely, similar studies utilizing natural sunlight as the source of irradiation indicated that phenol concentrations in solutions of pure water remained unchanged after ten days (Wilbaut-Isebree, 1964). However, phenol degradation did occur in industrial sewage effluents and led to the conclusion that unidentified microorganisms, not sunlight, were responsible for the destruction of phenol.

The microbiological degradation of phenol has been widely studied. Bayly, et al. (1966) reported the conversion of phenol to catechol by Pseudomonas putida. Neujahr and Varga (1970) observed the oxidation of phenol by both intact cells and extracts of the microorganism, Trichosporon cutaneum. Buswell and Twomey (1975) and Buswell (1975) demonstrated the ability of the thermophilic bacteria, Bacillus stearothermophilus, to catabolize phenol. In these studies, the bacteria first converted phenol to catechol and

subsequently cleaved the aromatic ring to form 2-hydroxymuconic semialdehyde. In view of the fact that phenol represented the primary carbon source provided to isolated and adapted microorganisms in these studies, the importance or microbiological degradation within the environment remains unclear.

Information concerning the presence and persistence, and fate of phenol in the environment is incomplete or not available.

The widespread use of phenol as an important chemical intermediate, the generation of phenolic wastes by industry and agriculture, and the toxicological and organoleptic properties indicate its importance in potential point source and nonpoint source water contamination.

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Aquatic Life Toxicology*

INTRODUCTION

Phenol is predominantly used as an intermediate in a wide variety of chemical processes. These processes produce epoxy and phenolic resins, pharmaceuticals, germicides, fungicides, slimicides, herbicides, dyes, and a variety of industrially important acids. The phenol molecule easily substitutes in the environment to form compounds such as halophenols, which may be more toxic than the parent molecule. Phenol is degraded by a number of bacteria and fungi that may cause slime growths and may depress dissolved oxygen in the receiving waters, thus lowering water quality.

Although an abundance of data on the acute toxicity of phenol to freshwater fish and invertebrate species is available, the chronic toxicity data are limited to one test with the fathead minnow. Toxicity testing with the same species by different researchers in different waters produced LC_{50} values which varied widely. This indicates that parameters such as pH, hardness, temperature or other water quality characteristics may alter the toxicity of the compound.

The data base for saltwater species is much more limited with acute data for three fish and three invertebrate species. No chronic data are available.

EFFECTS

Acute Toxicity

Toxicity data for eight freshwater invertebrate species, including a

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life and Its Uses in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are calculations for deriving various measures of toxicity as described in the Guidelines.

rotifer, a snail, cladocerans, and copepods, are listed in Table 1. Tests conducted by Alekseyev and Antipin (1976) compare the relative sensitivity of three cladoceran species in the same water using similar test methods. The LC_{50} values range from 14,000 µg/l for Daphnia longispina to 57,000 µg/l for Polyphemus pediculus. Data in Table 1 indicate that a rotifer, Philodina acuticornis, and two species of copepods are among the least sensitive. Cairns, et al. (1978) tested phenol at different temperatures and found little, if any, effect. LC_{50} values were in the range from 91,000 to 100,000 µg/l for Daphnia magna and 79,000 to 93,000 µg/l for Daphnia pulex. Anderson, et al. (1948) and Dowden and Bennett (1965) found young Daphnia magna to be about three times more sensitive than adults.

Acute toxicity data for nine freshwater fish species are included in Table 1. Rainbow trout was the most sensitive fish species tested with an LC_{50} value of 5,020 µg/l (McLeay, 1976). The least sensitive species was the fathead minnow with LC_{50} concentrations as high as 67,500 µg/l (U.S. EPA, 1978b). There is a wide range of intraspecific sensitivity in addition to the wide range of interspecific sensitivity previously mentioned. LC_{50} values for rainbow trout varied from 5,020 µg/l (McLeay, 1976) to 11,600 µg/l (Fogels and Sprague, 1977). The fathead minnow, a commonly used test species, had LC_{50} values that varied from 24,000 µg/l (Ruesink and Smith, 1975) to 67,500 µg/l (U.S. EPA, 1978b). The bluegill, another commonly used test species, had LC_{50} values from 11,500 µg/l (Cairns and Scheier, 1959) to 28,116 µg/l (Cairns, et al. 1978).

Only four saltwater species have been tested using standard test duration. Fifty percent effect levels for embryos of the eastern oyster and hard clam were 58,250 and 52,630 µg/l, respectively (Table 1). The grass shrimp was much more sensitive with an LC_{50} of 5,800 µg/l. The mountain bass, a species endemic to Hawaii, provided a 96-hour LC_{50} value of 11,000

ug/l (Table 1). There are too few data to evaluate any effect of environmental variables on toxicity.

Chronic Toxicity

An early life stage test with the fathead minnow (Holcombe, et al. 1980) produced an estimated maximum acceptable toxicant concentration of 1,830 to 3,570 ug/l which yields a chronic value of 2,560 ug/l and an acute-chronic ratio of 14 (Table 2). Species mean acute values and the acute-chronic ratio are summarized in Table 3.

No chronic effects are available for any saltwater species.

Plant Effects

Reynolds, et al. (1973) conducted a series of tests with an alga, Selenastrum capricornutum, and found at phenol concentrations of 20,000 ug/l that growth inhibition increased from 12 percent to 32 percent as temperature increased from 20 to 28°C (Table 4). Reynolds, et al. (1975) found greater than 50 percent reduction in cell numbers of the same alga at 20,000 ug/l in 1.92, 2.0, and 2.26 days at 20, 24, and 28°C, respectively. Duckweed was considerablely less sensitive with an LC_{50} of 1,504,000 ug/l (Blackman, et al. 1955) and 50 percent reduction in growth at 479,400 ug/l (Simon and Blackman, 1953).

Residues

Table 5 contains bioconcentration data on phenol for goldfish. However, since no maximum permissible tissue concentration is available for phenol, no Final Residue Value can be calculated. The bioconcentration factors calculated for phenol (Kobayashi, et al. 1976, Kobayashi and Akitake, 1975) ranged from 1.2 to 2.3. Bioconcentration factors this low indicate that no residue problem should occur from exposure to phenol.

Miscellaneous

Birge, et al. (1979) conducted tests at hardnesses of 50 and 200 mg/l

as $CaCO_3$ and determined 4-day LC_{50} values for three species of fishes after exposure of the entire embryo stage and four days of the larval life stage. LC_{50} values for rainbow trout were 310 and 70 µg/l, for goldfish, 840 and 340 µg/l, and for bluegills 2,420 and 1,690 µg/l in soft and hard water, respectively. The tests indicate that hardness may affect the toxicity of phenol although related characteristics may be the factor.

Cairns, et al. (1978) in tests conducted with rainbow trout at 5, 12, and 18°C calculated 24-hour LC_{50} values of 5,600, 11,000, and 11,300 µg/l, respectively. The tests indicate that rainbow trout are about twice as sensitive at 5°C than at 12 and 18°C.

Mitrovic, et al. (1968) detected gill damage in rainbow trout juveniles in 2 hours at a concentration of 6,500 µg/l. However, it is difficult to understand the environmental significance of this because of possible compensatory reactions in the fish.

Histopathological damage occurred in the saltwater clam, Mercenaria mercenaria, at phenol concentrations of 100 µg/l and higher (Table 6). No change was observed at 10 µg/l.

The saltwater mountain bass reacted to phenol concentrations as low as 2,000 µg/l, and the 48-hour LC_{50} for the rainbow trout in saltwater was 6,900 µg/l (Table 6).

Summary

The acute toxicity of phenol to freshwater species is expressed over a range of 2 to 3 orders of magnitude. Of the four families of invertebrate species represented, the cladocerans were the most sensitive. Acute values for fish species range from 67,500 µg/l for fathead minnows to 5,020 µg/l for juvenile rainbow trout. The acute value for rainbow trout of 5,020 µg/l and the value of 5,000 µg/l for Daphnia magna are the lowest acute values observed.

A fathead minnow early life stage test resulted in a chronic value of 2,560 ug/l with an acute-chronic ratio of 14.

Bioconcentration factors ranged from 1.2 to 2.3 in goldfish in five days. Factors this low indicate that no residue problem should occur from exposure to phenol.

Only three saltwater invertebrate and three fish species have been studied as to the acute effects of phenol. LC_{50} values were observed as low as 5,800 ug/l. Histopathological damage was observed in the hard clam at concentrations as low as 100 ug/l. A saltwater fish reacted to concentrations as low as 2,000 ug/l.

CRITERIA

The available data for phenol indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 10,200 and 2,560 ug/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for phenol indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 5,800 ug/l and would occur at lower concentrations among species that are more sensitive than those tested. No data are available concerning the chronic toxicity of phenol to sensitive saltwater aquatic life.

Table 1. Acute values for phenol

Species	Method[a]	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
		FRESHWATER SPECIES		
Rotifer, *Philodina acuticornis*	S, U	248,000	248,000	Bulkema, et al. 1974
Snail, *Physa heterostropha*	S, U	94,000	94,000	Patrick, et al. 1968
Cladoceran, *Daphnia longispina*	R, U	14,000	14,000	Alekseyev & Antipin, 1976
Cladoceran, *Daphnia magna*	S, U	9,600	-	Kopperman, et al. 1974
Cladoceran, *Daphnia magna*	S, U	11,800	-	U.S. EPA, 1978a
Cladoceran (young), *Daphnia magna*	S, U	7,000	-	Dowden & Bennett, 1965
Cladoceran (adult), *Daphnia magna*	S, U	21,000	-	Dowden & Bennett, 1965
Cladoceran, *Daphnia magna*	S, M	100,000	-	Cairns, et al. 1978
Cladoceran, *Daphnia magna*	S, M	92,000	-	Cairns, et al. 1978
Cladoceran, *Daphnia magna*	S, M	91,000	-	Cairns, et al. 1978
Cladoceran, *Daphnia magna*	S, M	88,000	-	Cairns, et al. 1978
Cladoceran, *Daphnia magna*	S, M	91,200	36,400	Cairns, et al. 1978
Cladoceran, *Daphnia pulex*	S, U	28,000	-	Lee, 1976

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Cladoceran, *Daphnia pulex*	S, M	93,000	-	Cairns, et al. 1978
Cladoceran, *Daphnia pulex*	S, M	87,800	-	Cairns, et al. 1978
Cladoceran, *Daphnia pulex*	S, M	85,000	-	Cairns, et al. 1978
Cladoceran, *Daphnia pulex*	S, M	81,000	-	Cairns, et al. 1978
Cladoceran, *Daphnia pulex*	S, M	79,000	-	Cairns, et al. 1978
Cladoceran, *Daphnia pulex*	R, U	18,000	58,100	Alekseyev & Antipin, 1976
Cladoceran, *Polyphemus pediculus*	R, U	57,000	57,000	Alekseyev & Antipin, 1976
Copepod, *Cyclops vernalis*	S, U	122,000	122,000	Anderson, et al. 1948
Copepod, *Mesocyclops leukarti*	S, U	108,000	108,000	Anderson, et al. 1948
Rainbow trout (juvenile), *Salmo gairdneri*	R, U	5,020	-	McLeay, 1976
Rainbow trout (juvenile), *Salmo gairdneri*	FT, M	8,900	-	U.S. EPA, 1978b
Rainbow trout, *Salmo gairdneri*	FT, M	11,600	10,200	Fogels & Sprague, 1977
Goldfish, *Carassius auratus*	S, U	44,490	44,500	Pickering & Henderson, 1966
Fathead minnow (adult), *Pimephales promelas*	FT, M	67,500	-	U.S. EPA, 1978b

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Fathead minnow, *Pimephales promelas*	S, U	34,270	-	Pickering & Henderson, 1966
Fathead minnow, *Pimephales promelas*	S, U	32,000	-	Pickering & Henderson, 1966
Fathead minnow (adult), *Pimephales promelas*	FT, M	36,000	-	Ruesink & Smith, 1975
Fathead minnow (adult), *Pimephales promelas*	FT, M	24,000	-	Ruesink & Smith, 1975
Fathead minnow, *Pimephales promelas*	FT, M	28,780	-	Phipps, et al. Manuscript
Fathead minnow, *Pimephales promelas*	S, U	32,000	36,000	Mattson, et al. 1976
Channel catfish (juvenile), *Ictalurus punctatus*	S, U	16,700	16,700	Clemens & Sneed, 1959
Flagfish, *Jordanella floridae*	FT, M	36,300	36,300	Fogels & Sprague, 1977
Mosquitofish, *Gambusia affinis*	S, M	26,000	26,000	Nunogawa, et al. 1970
Guppy, *Poecilia reticulata*	S, M	31,000	-	Nunogawa, et al. 1970
Guppy, *Poecilia reticulata*	S, U	39,190	34,900	Pickering & Henderson, 1966
Bluegill, *Lepomis macrochirus*	S, U	13,500	-	Patrick, et al. 1968
Bluegill (juvenile), *Lepomis macrochirus*	R, M	19,300	-	Trama, 1955
Bluegill, *Lepomis macrochirus*	S, U	13,500	-	Cairns & Scheier, 1959

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Bluegill, Lepomis macrochirus	S, U	20,000	-	Cairns & Scheier, 1959
Bluegill, Lepomis macrochirus	S, U	11,500	-	Cairns & Scheier, 1959
Bluegill, Lepomis macrochirus	S, U	23,880	16,400	Pickering & Henderson, 1966
Mozambique mouthbrooder, Tilapia mossambica	S, M	19,000	19,000	Nunogawa, et al. 1970
		SALTWATER SPECIES		
Grass shrimp, Palaemonetes pugio	S, U	5,800	5,800	Tatem, et al. 1978
Eastern oyster, Crassostrea virginica	S, U	58,250	58,200	Davis & Hidu, 1969
Hard clam, Mercenaria mercenaria	S, U	52,630	52,600	Davis & Hidu, 1969
Mountain bass, Kuhlia sandvicensis	S, M	11,000	11,000	Nunogawa, et al. 1970

* S = static, R = renewal, FT = flow-through, U = unmeasured, M = measured

Table 2. Chronic values for phenol (Holcombe, et al. 1980)

Species	Method*	Limits (µg/l)	Chronic Value (µg/l)
FRESHWATER SPECIES			
Fathead minnow, *Pimephales promelas*	ELS	1,830–3,570	2,560

* ELS = early life stage

Acute-Chronic Ratio

Species	Acute Value (µg/l)	Chronic Value (µg/l)	Ratio
Fathead minnow, *Pimephales promelas*	36,000	2,560	14

Table 3. Species mean acute values and acute-chronic ratios for phenol

Rank*	Species	Species Mean Acute Value (µg/l)	Acute-Chronic Ratio
		FRESHWATER SPECIES	
17	Rotifer, *Philodina acuticornis*	248,000	-
16	Copepod, *Cyclops vernalis*	122,000	-
15	Copepod, *Mesocyclops leukarti*	108,000	-
14	Snail, *Physa heterostropha*	94,000	-
13	Cladoceran, *Daphnia pulex*	58,100	-
12	Cladoceran, *Polyphemus pediculus*	57,000	-
11	Goldfish, *Carassius auratus*	44,500	-
10	Cladoceran, *Daphnia magna*	36,390	-
9	Flagfish, *Jordanella floridae*	36,300	-
8	Fathead minnow, *Pimephales promelas*	36,000	14
7	Guppy, *Poecilia reticulata*	34,900	-
6	Mosquitofish, *Gambusia affinis*	26,000	-
5	Mozambique mouthbrooder, *Tilapia mossambica*	19,000	-
4	Channel catfish, *Ictalurus punctatus*	16,700	-

Table 3. (Continued)

Rank*	Species	Species Mean Acute Value (µg/l)	Acute-Chronic Ratio
3	Bluegill, *Lepomis macrochirus*	16,400	-
2	Cladoceran, *Daphnia longispina*	14,000	-
1	Rainbow trout, *Salmo gairdneri*	10,200	-
	SALTWATER SPECIES		
4	Eastern oyster, *Crassostrea virginica*	58,200	-
3	Hard clam, *Mercenaria mercenaria*	52,600	-
2	Mountain bass, *Kuhlia sandvicensis*	11,000	-
1	Grass shrimp, *Palaemonetes pugio*	5,800	-

* Ranked from least sensitive to most sensitive by species mean acute value.

Table 4. Plant values for phenol

Species	Effect	Result (µg/l)	Reference
	FRESHWATER SPECIES		
Alga, *Selenastrum capricornutum*	12% growth inhibition at 20 C	20,000	Reynolds, et al. 1973
Alga, *Selenastrum capricornutum*	27% growth inhibition at 24 C	20,000	Reynolds, et al. 1973
Alga, *Selenastrum capricornutum*	32% growth inhibition at 28 C	20,000	Reynolds, et al. 1973
Alga, *Selenastrum capricornutum*	>50% reduction of 1-day steady state cell concentration	40,000	Reynolds, et al. 1975
Alga, *Selenastrum capricornutum*	58% reduction in cell numbers in 1.92 days at 20 C	20,000	Reynolds, et al. 1975
Alga, *Selenastrum capricornutum*	66% reduction in cell numbers in 2.0 days at 24 C	20,000	Reynolds, et al. 1975
Alga, *Selenastrum capricornutum*	60% reduction in cell numbers in 2.26 days at 28 C	20,000	Reynolds, et al. 1975
Duckweed, *Lemna minor*	Chlorosis (LC50)	1,504,000	Blackman, et al. 1955
Duckweed, *Lemna minor*	50% reduction in growth	479,400	Simon & Blackman, 1953

Table 5. Residues for phenol

Species	Tissue	Bioconcentration Factor	Duration (days)	Reference
		FRESHWATER SPECIES		
Goldfish, Carassius auratus	Whole body	2.0	1	Kobayashi, et al. 1976
Goldfish, Carassius auratus	Whole body	2.0	5	Kobayashi & Akitake, 1975
Goldfish, Carassius auratus	Whole body	1.2-2.3	5	Kobayashi & Akitake, 1975

Table 6. Other data for phenol

Species	Duration	Effect	Result (µg/l)	Reference
		FRESHWATER SPECIES		
Diatom, *Nitzschia linearis*	120 hrs	50% reduction in cell production	258,000	Patrick, et al. 1968
Alga, *Chlorella pyrenaidosa*	2 days	Complete destruction of chlorophyll	1,500,000	Huang & Gloyna, 1968
Alga, *Chlorella vulgaris*	80 hrs	20% inhibition of growth	470,000	Dedonder & Van Sumere, 1971
Paramecium, *Chilomonas paramecium*	19-25 hrs	>50% decrease in growth	200,000	Cairns, et al. 1978
Paramecium, *Chilomonas paramecium*	44-48 hrs	>50% decrease in growth	200,000	Cairns, et al. 1978
Paramecium, *Chilomonas paramecium*	98-163 hrs	>50% decrease in growth	200,000	Cairns, et al. 1978
Rotifer, *Philodina acuticornis*	48 hrs	LC50	300,000	Cairns, et al. 1978
Rotifer, *Philodina acuticornis*	48 hrs	LC50	282,000	Cairns, et al. 1978
Rotifer, *Philodina acuticornis*	48 hrs	LC50	245,000	Cairns, et al. 1978
Rotifer, *Philodina acuticornis*	48 hrs	LC50	205,000	Cairns, et al. 1978
Rotifer, *Philodina acuticornis*	48 hrs	LC50	292,000	Cairns, et al. 1978
Annelid, *Aeolosoma headleyi*	48 hrs	LC50	360,000	Cairns, et al. 1978
Annelid, *Aeolosoma headleyi*	48 hrs	LC50	351,000	Cairns, et al. 1978

Table 6. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Annelid, *Aeolosoma headleyi*	48 hrs	LC50	381,000	Cairns, et al. 1978
Annelid, *Aeolosoma headleyi*	48 hrs	LC50	356,000	Cairns, et al. 1978
Annelid, *Aeolosoma headleyi*	48 hrs	LC50	341,000	Cairns, et al. 1978
Snail, *Limnaea stagnalis*	48 hrs	LC50	350,000	Alekseyev & Antipin, 1976
Snail, *Nitrocris* sp.	48 hrs	LC50	389,000	Cairns, et al. 1978
Snail, *Nitrocris* sp.	48 hrs	LC50	351,000	Cairns, et al. 1978
Snail, *Nitrocris* sp.	48 hrs	LC50	353,000	Cairns, et al. 1978
Snail, *Nitrocris* sp.	48 hrs	LC50	360,000	Cairns, et al. 1978
Snail, *Nitrocris* sp.	48 hrs	LC50	391,000	Cairns, et al. 1978
Snail (adult), *Physa fontinalis*	48 hrs	LC50	320,000	Alekseyev & Antipin, 1976
Snail (juvenile), *Physa fontinalis*	48 hrs	LC50	260,000	Alekseyev & Antipin, 1976
Clam, *Sphaerium corneum*	48 hrs	LC50	780,000	Alekseyev & Antipin, 1976
Cladoceran, *Daphnia magna*	16 hrs	Immobilization	94,000	Anderson, 1944
Cladoceran (young), *Daphnia magna*	96 hrs	EC50	5,000	Anderson, et al. 1948

Table 6. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Cladoceran (adult), *Daphnia magna*	96 hrs	EC50	14,000	Anderson, et al. 1948
Conchostracan, *Lynceus brachyurus*	48 hrs	LC50	78,000	Alekseyev & Antipin, 1976
Isopod (adult), *Asellus aquaticus*	48 hrs	LC50	15,000	Alekseyev & Antipin, 1976
Isopod (juvenile), *Asellus aquaticus*	48 hrs	LC50	78,000	Alekseyev & Antipin, 1976
Rainbow trout, *Salmo gairdneri*	48 hrs	LC50	10,200	Alexander & Clarke, 1978
Rainbow trout, *Salmo gairdneri*	48 hrs	LC50	10,400	Alexander & Clarke, 1978
Rainbow trout, *Salmo gairdneri*	48 hrs	LC50	9,000	Alexander & Clarke, 1978
Rainbow trout, *Salmo gairdneri*	48 hrs	LC50	9,600	Alexander & Clarke, 1978
Rainbow trout, *Salmo gairdneri*	48 hrs	LC50	9,500	Alexander & Clarke, 1978
Rainbow trout, *Salmo gairdneri*	48 hrs	LC50	9,200	Alexander & Clarke, 1978
Rainbow trout (embryo), *Salmo gairdneri*	22 days	LC50 (hardness = 50 mg/l $CaCO_3$)	330	Birge, et al. 1979
Rainbow trout (embryo), *Salmo gairdneri*	22 days	LC50 (hardness = 200 mg/l $CaCO_3$)	70	Birge, et al. 1979
Rainbow trout, *Salmo gairdneri*	26 days	LC50 (hardness = 50 mg/l $CaCO_3$)	310	Birge, et al. 1979
Rainbow trout, *Salmo gairdneri*	26 days	LC50 (hardness = 200 mg/l $CaCO_3$)	70	Birge, et al. 1979

Table 6. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Rainbow trout (juvenile), Salmo gairdneri	48 hrs	50% mortality	5,400	Brown, et al. 1967b
Rainbow trout (juvenile), Salmo gairdneri	48 hrs	50% mortality	8,000	Brown, et al. 1967b
Rainbow trout (juvenile), Salmo gairdneri	48 hrs	50% mortality	9,800	Brown, et al. 1967b
Rainbow trout (juvenile), Salmo gairdneri	48 hrs	50% mortality	7,500	Mitrovic, et al. 1968
Rainbow trout (yearling), Salmo gairdneri	48 hrs	50% mortality	9,400	Brown & Dalton, 1970
Rainbow trout, Salmo gairdneri	24 hrs	50% mortality	5,600	Cairns, et al. 1978
Rainbow trout, Salmo gairdneri	24 hrs	50% mortality	11,000	Cairns, et al. 1978
Rainbow trout, Salmo gairdneri	24 hrs	50% mortality	11,300	Cairns, et al. 1978
Rainbow trout, Salmo gairdneri	114 min	50% mortality	12,200	Herbert, 1962
Rainbow trout (juvenile), Salmo gairdneri	2 hrs	Gill damage	6,500	Mitrovic, et al. 1968
Rainbow trout, Salmo gairdneri	48 hrs	Lowest concentration which killed 50% or more of the test fish	10,000	Shumway & Palensky, 1973
Brook trout (juvenile), Salvelinus fontinalis	24 hrs	Temperature selection shifted significantly downward	7,500	Miller & Ogilvie, 1975
Brook trout (juvenile), Salvelinus fontinalis	24 hrs	50% mortality	11,700	Miller & Ogilvie, 1975

Table 6. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Goldfish, *Carassius auratus*	8 hrs	LC62	33,300	Gersdorff, 1939
Goldfish, *Carassius auratus*	8 hrs	LC67	41,600	Gersdorff & Smith, 1940
Goldfish, *Carassius auratus*	24 hrs	50% mortality	200,000	Cairns, et al. 1978
Goldfish, *Carassius auratus*	20-30 hrs	50% mortality	40,000-100,000	Kobayashi & Akitake, 1975
Goldfish (embryo), *Carassius auratus*	3.5 days	LC50 (hardness = 50 mg/l $CaCO_3$)	1,220	Birge, et al. 1979
Goldfish (embryo), *Carassius auratus*	3.5 days	LC50 (hardness = 200 mg/l $CaCO_3$)	390	Birge, et al. 1979
Goldfish, *Carassius auratus*	7.5 days	LC50 (hardness = 50 mg/l $CaCO_3$)	840	Birge, et al. 1979
Goldfish, *Carassius auratus*	7.5 days	LC50 (hardness = 200 mg/l $CaCO_3$)	340	Birge, et al. 1979
Goldfish, *Carassius auratus*	24 hrs	LC50	60,000	Kobayashi, et al. 1979
Golden shiner, *Notemigonius crysoleueus*	24 hrs	50% mortality	129,000	Cairns, et al. 1978
Golden shiner, *Notemigonius crysoleueus*	24 hrs	50% mortality	35,000	Cairns, et al. 1978
Fathead minnow (adult), *Pimephales promelas*	24 hrs	50% mortality	65,340	Jenkins, 1960
Fathead minnow (adult), *Pimephales promelas*	216 hrs	Median lethal threshold	27,000	Ruesink & Smith, 1975
Fathead minnow (adult), *Pimephales promelas*	122-127 hrs	Median lethal threshold	22,000	Ruesink & Smith, 1975

Table 6. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Walking catfish, Clarias batrachus	48 hrs	50% mortality	31,500	Mukherjee & Bhattacharya, 1974
Guppy (adult), Poecilia reticulata	30 days	Increase in neurosecratory hormone	3,120	Matei & Fierov, 1973
Mollies (adult), Mollienesia latipinna	25 hrs	50% mortality	63,000	Dowden & Bennett, 1965
Mollies (adult), Mollienesia latipinna	50 hrs	50% mortality	22,000	Dowden & Bennett, 1965
Bluegill, Lepomis macrochirus	25 hrs	50% mortality	10,000-15,000	Dowden & Bennett, 1965
Bluegill (juvenile), Lepomis macrochirus	48 hrs	50% mortality	22,200	Lammering & Burbank, 1960
Bluegill (juvenile), Lepomis macrochirus	48 hrs	50% mortality	19,000	Turnbull, et al. 1954
Bluegill, Lepomis macrochirus	24 hrs	50% mortality	60,000	Cairns, et al. 1978
Bluegill (embryo), Lepomis macrochirus	2.5 days	LC50 (hardness = 50 mg/l $CaCO_3$)	3,340	Birge, et al. 1979
Bluegill (embryo), Lepomis macrochirus	2.5 days	LC50 (hardness = 200 mg/l $CaCO_3$)	2,430	Birge, et al. 1979
Bluegill, Lepomis macrochirus	6.5 days	LC50 (hardness = 50 mg/l $CaCO_3$)	2,420	Birge, et al. 1979
Bluegill, Lepomis macrochirus	6.5 days	LC50 (hardness = 200 mg/l $CaCO_3$)	1,690	Birge, et al. 1979
Mozambique mouthbrooder, Tilapia mossambica	1 mo	Manifest hemosiderosis in the spleen	2,000	Murachi, et al. 1974

Table 6. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
		SALTWATER SPECIES		
Hard clam (adult), Mercenaria mercenaria	24 hrs	Cellular damage	100	Fries & Tripp, 1977
Hard clam (adult), Mercenaria mercenaria	24 hrs	No cellular damage	10	Fries & Tripp, 1977
Mountain bass, Kuhlia sandvicensis	Acute	Violent reaction	20,000	Hiatt, et al. 1953
Mountain bass, Kuhlia sandvicensis	Acute	Moderate reaction	2,000	Hiatt, et al. 1953
Nehu, Stolephorus purpureus	12 hrs	LC50	510	Nunogawa, et al. 1970
Rainbow trout, Salmo gairdneri	48 hrs	LC50	6,900	Brown, et al. 1967a

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Mammalian Toxicology and Human Health Effects

INTRODUCTION

Phenol is a high-volume industrial chemical which is widely used as an intermediate in the manufacture of other chemicals. Phenol is also produced by biological processes and is a by-product of combustion and some industrial processes.

Phenol exists at 25°C as a clear, colorless, hygroscopic, deliquescent, crystalline solid which may become slightly pink in color as a result of impurities (Lederman and Poffenberger, 1968). The chemical and physical characteristics of phenol are presented in Table 1.

Phenol has a long history of industrial and medical use. In 1867, Lister reported on the use of phenol sprays for disinfecting operating rooms. Today its medicinal uses are limited to a few mouth, throat, and skin medications. The industrial capacity for the production of phenol in the United States was $2,885 \times 10^6$ pounds per year in 1975 (Anonymous, 1975); about 90 percent of the phenol produced that year was used in the production of phenolic resins, caprolactam, bisphenol-A, alkylphenols, and adipic acid (Chemical Profiles, 1972). Phenol is highly soluble in water under ambient conditions.

It should be noted that analytical data for phenol should be interpreted with caution. Many spectrophotometric tests, specifically those following the methodologies presented by Deichmann (1942) are positive for phenol as well as a spectrum of substituted phenol compounds (Am. Pub. Health Assoc., 1971; Ettinger, et al. 1951; Smith, 1976).

TABLE 1

Chemical and Physical Properties of Phenol*

Formula:	C_6H_5OH
Molecular weight:	94.11
pK_a:	9.9
Melting point:	40-41°C
Boiling point:	181.75°C
Vapor pressure @ 25°C	0.35 mm Hg
Specific gravity: solid @ 25°C	1.071
liquid @ 25°C	1.049
Relative vapor density: (air = 1.0)	3.24
Solubility: (X = mole fraction) Phenol in water: -log X = 0.375 log(66 - T) + 1.15. Water in phenol: -log X = -0.62 log(66 - T) + 0.99	Also soluble in ether, alcohol, acetic acid, glycerol, liquid sulfur dioxide, benzene.
Color:	Colorless to light pink solid
Odor:	Sweet; threshold = 1ppm
Flashpoint: open cup	85°C
closed cup	79°C
Ignition temperature:	715°C
Light sensitivity:	Darkens on exposure to light
Saturated vapor concentration (25°C):	461 ppm

*Source: NIOSH, 1976

The National Organic Monitoring Survey (U.S. EPA, 1977) reported finding unspecified concentrations of phenol in 2 out of 110 raw water supplies. The survey found no phenol in any finished water supplies. The National Commission on Water Quality (1975) reported from U.S. Geological Survey data that the annual mean concentration of phenol in the lower Mississippi River was 1.5 µg/l, with a maximum of 6.7 µg/l and a minimum of 0.0 µg/l. The International Joint Commission (1978) reported finding $\leq$0.5 to 5 µg/l phenol in the Detroit river between 1972 and 1977.

Phenol is also produced endogenously in the mammalian intestinal tract through the microbial metabolism of l-tyrosine and p-hydroxybenzoic acid (Harborne, 1964). In addition, exposures to benzene (Docter and Zielhuis, 1967) and the ingestion of certain drugs (Fishbeck, et al. 1975) can lead to increased phenol production and excretion.

EXPOSURE

Ingestion from Water

As noted previously, during the National Organic Monitoring Survey (U.S. EPA, 1977), phenol was found in only 2 of 110 raw water supplies analyzed by gas-liquid chromatography and mass spectrometry; however, in the two instances in which the presence of phenol was detected, no quantification was made. No phenol was found in finished water supplies. The National Commission on Water Quality (1975) reported an annual mean concentration of 1.5 µg/l of phenol in raw water from the lower Mississippi River. At a water intake of 2 liters per day, this would result in a phenol intake of 3 µg/person/day.

A 1974 train derailment in southern Wisconsin resulted in significant groundwater contamination by phenol (Delfino and Dube, 1976; Baker, et al. 1978). Most families in the area of the spill continued drinking their well water until it became unpalatable. The maximum concentration of phenol in the contaminated water actually ingested by the 39 victims is uncertain. The first tests revealed phenol concentrations of 0.21 to 3.2 mg/l in nearby wells. Concentrations in the well water eventually reached a maximum of 1,130 mg/l. Baker, et al. (1978) estimated exposures of 10 to 240 mg/person/day in the highest exposure group. Medical histories taken six months after the spill showed a statistically significant increase in reported cases of diarrhea, mouth sores, dark urine, and burning of the mouth. Laboratory tests done at this same time for serum glutamic oxalacetic transaminase (SGOT), bilirubin, creatinine, uric acid, glucose, and cholesterol showed no significant abnormalities. Six months after each group's initial exposure, urinary free and conjugated phenol levels were 11.97 mg/l for the study group and 11.56 mg/l for the control group, indicating that the metabolism of dietary constituents, rather than the ingestion of contaminated water, contributed to the phenol found in the urine at that time.

Prior to 1900, phenol was frequently ingested to commit suicide (von Oettingen, 1949). Reported lethal doses in man ranged from 4.8 to 128.0 grams [National Institute for Occupational Safety Health (NIOSH), 1976].

Ingestion from Food

Free and conjugated phenol are normal constituents of animal matter (Table 2). They are most likely formed in the intestinal tract by microbial metabolism of l-tyrosine and p-hydroxybenzoic acid (von Oettingen, 1949; Harborne, 1964). There are no market basket surveys of free and conjugated phenol to allow an estimate of the daily dietary intake of phenol. Lustre and Issenberg (1970) have reported finding 7 mg phenol/kg in smoked summer sausage and 28.6 mg/kg in smoked pork belly.

Four medicinal preparations which could be expected to contribute to the ingestion of phenol are presently on the market. They are Cepastat® Mouthwash and Cepastat® Lozenges, containing 1.45 percent phenol; Chloraseptic® Mouthwash, containing 1.4 percent phenol; and Chloraseptic® Lozenges, containing 32.5 mg total phenol (free phenol and sodium phenolate) per lozenge with a total manufacturer's recommended dose of up to eight lozenges per day (Huff, 1978). Because there is no control over the intake of non-prescription drugs, some individuals may consume considerably higher doses.

The taste and odor of phenol, and particularly of some of its derivatives, are noticeable at relatively low concentrations (Table 3).

In a study conducted at the Mellon Institute in Pittsburg, Pennsylvania, by Hoak (1957), a panel of 2 or 4 persons sniffed samples of pure phenolic compounds in odor-free water, which had been heated to 30 to 60°C. A flask of plain odor-free water was provided for comparison. The various samples were placed in random

TABLE 2

Phenol Content of Normal Rabbit Tissues*
(6 animals)

Tissue	Phenol (mg/kg)		
	Free	Conjugated	Total
Blood	0-0.7	0-0.5	0-0.7
CNS	0	0-1.8	0-1.8
Kidney	0-1.0	0-0.5	0-1.4
Lung	0-2.3	0-3.4	0-3.4
Liver	0-0.9	1.1-5.5	1.1-6.2
Muscle	0-1.6	0-1.8	0-3.4
G.I. Tract (including contents)	0-3.0	0-2.3	0-4.4
Heart, spleen, thymus, testes, adrenals	0-0.3	0-1.0	0-1.0
Urine (24 hr. vol.)	0-3.9	11.5-100.0	11.5-100.0
Feces (24 hr.)	0.4-5.3	1.4-8.0	1.8-11.7

*Source: Deichmann, 1944.

TABLE 3

Taste and Odor Thresholds for Phenol in Water

Taste mg/l	Odor mg/l	Temperature °C	Reference
>1.0	>1.0	ca.24	Burttschell, et al. 1959
0.3	4.0	20-22	Dietz and Traud, 1978
60	-	-	Campbell, et al. 1958
-	10.0	30	Hoak, 1957
-	5.0	60	Hoak, 1957
1.0	1.0	-	Veldrye, 1972

order before the test persons, and the flask with the lowest perceptible odor was noted by each individual sniffer. The lowest concentration detected was considered to be the threshold. Of the chemicals tested, chlorinated phenols were the compounds most easily detected. The odor thresholds reported for phenol were 10 µg/l at 30°C and 5 µg/l at 60°C. Hoak (1957) speculated that odor should be expected to become more noticeable as temperature increases; however, in evaluating phenol and a series of chlorophenols and cresols, it was found that some compounds had higher odor thresholds at 30°C, while others were higher at 60°C.

Burttschell, et al. (1959) made dilutions of phenolic compounds in carbon-filtered tap water and used a panel of from 4 to 6 persons to evaluate odor and taste. Tests were carried out at room temperature, which the investigator estimated to be 25°C. If a panel member's response was doubtful, the sample was considered negative. The geometric means ($\geq$1,000 µg/l for odor and taste) of the panel responses were used as the organoleptic thresholds. The data presented did not indicate a range of responses.

Campbell, et al. (1958) studied the taste thresholds of six odor-producing chemicals including phenol. Solutions of the chemicals were prepared using redistilled water. Panels of 21 to 22 experienced judges participated in different organoleptic tests of the triangle type. Concentrations of chemicals chosen for the triangle tests were such that the odd sample would be identified by more than 35, but less than 100 percent of the judges. Samples were served in 25 ml portions, and the judges were asked only to iden-

tify the odd sample. When 50 percent of the judges correctly separated the samples in a given triangle test, the concentration of compound used in that test was considered to be the threshold level. Although a number of judges were able to detect the presence of phenol at a concentration of 14 mg/l, a threshold level of 60 mg/l was reported based upon the experimental methodology used.

Dietz and Traud (1978) used a panel composed of 9 to 12 persons of both sexes and various age groups to test the organoleptic detection thresholds for 126 phenolic compounds. To test for odor thresholds, 200 ml samples of the different test concentrations were placed in stoppered odor-free glass bottles, shaken for approximately five minutes, and sniffed at room temperature (20 to 22^{o}C). For each test, water without the phenolic additive was used as a background sample. The odor tests took place in several individual rooms in which phenols and other substances with intense odors had not been used previously. Geometric mean values were used to determine threshold levels. To determine taste threshold concentrations of selected phenolic compounds, a panel of four test individuals tasted water samples containing various amounts of phenolic additives. As a point of comparison, water without phenolic additives was tasted first. Samples with increasing phenolic concentrations were then tested. Between samples, the mouth was rinsed with the comparison water and the test person ate several bites of dry white bread to "neutralize" the taste. Geometric mean detection level values for both tests provided threshold levels of phenol of 0.3 mg/l for taste and 4.0 mg/l for odor.

None of the four organoleptic studies described, however, indicated whether the determined threshold levels made the water undesirable or unfit for consumption.

A bioconcentration factor (BCF) relates the concentrations of a chemical in aquatic animals to the concentration in the water in which they live. The steady-state BCFs for a lipid-soluble compound in the tissues of various aquatic animals seem to be proportional to the percent lipid in the tissue. Thus, the per capita ingestion of a lipid-soluble chemical can be estimated from the per capita consumption of fish and shellfish, the weighted average percent lipids of consumed fish and shellfish, and a steady-state BCF for the chemical.

Data from a recent survey on fish and shellfish consumption in the United States were analyzed by SRI International (U.S. EPA, 1980a). These data were used to estimate that the per capita consumption of freshwater and estuarine fish and shellfish in the United States is 6.5 g/day (Stephan, 1980). In addition, these data were used with data on the fat content of the edible portion of the same species to estimate that the weighted average percent lipids for consumed freshwater and estuarine fish and shellfish is 3.0 percent.

Measured BCFs of 1.2 to 2.3 were obtained with goldfish by Kobayashi, et al. (1976) and Kobayashi and Akitake (1975), but percent lipids was not measured. The equation "Log BCF = (0.85 Log P) - 0.70" can be used (Veith, et al. 1979) to estimate the BCF for aquatic organisms that contain about 7.6 percent lipids (Veith, 1980) from the octanol/water partition coefficient (P). Based on

an average measured log P value of 1.48 (Hansch and Leo, 1979), the steady-state BCF for phenol is estimated to be 3.6. An adjustment factor of 3.0/7.6 = 0.395 can be used to adjust the estimated BCF from the 7.6 percent lipids on which the equation is based to the 3.0 percent lipids that is the weighted average for consumed fish and shellfish. Thus, the weighted average BCF for phenol and the edible portion of all freshwater and estuarine aquatic organisms consumed by Americans is calculated to be 3.6 x 0.395 = 1.4.

Inhalation

The inhalation of phenol vapors appears to be largely restricted to the occupational environment. Phenol vapor is efficiently absorbed from the lungs. Piotrowski (1971) administered phenol vapors to human volunteers wearing masks to minimize the effect of skin absorption. The phenol concentrations ranged from 6 to 20 mg/m^3. Piotrowski (1971) found that the retention of phenol averaged 80 percent at the beginning of the exposure but decreased to an average retention of 70 percent after eight hours of exposure. He did not report any adverse effects in his subjects after the exposures to phenol vapor.

Ohtsuji and Ikeda (1972) found up to 12.5 mg/m^3 of phenol vapors in bakelite factories. They reported no adverse effects but confirmed that phenol was efficiently absorbed through the lungs.

The present threshold limit value (TLV) for phenol is 20 mg/m^3 as a time-weighted average (TWA) with a ceiling value of 60 mg/m^3 (NIOSH, 1976).

Dermal

The primary site of phenol absorption in industrial exposures is the skin. The skin is a major route of entry for phenol vapor,

phenol solutions, liquid phenol, or solid phenol. Piotrowski (1971) determined that the rate of absorption of phenol vapor through the skin was similar to that through the respiratory tract. Aqueous phenol solutions (1 percent w/v) readily penetrate human skin (Roberts, et al. 1977). As the phenol concentration increases, the permeability coefficient also increases. At very high concentrations of phenol in water, the resulting skin damage retards the absorption of phenol (Deichmann and Keplinger, 1963).

In addition to exposures from occupational sources, a number of medicinal preparations can be sources of dermally absorbed phenol. A partial census of phenol-containing preparations for skin application is as follows: Campho-Phenique® liquid - 4.75 percent phenol, powder - 2 percent; Calamine lotion, 1 percent phenol; P&S® ointment or liquid, 1 percent phenol; Panscol® ointment, 1 percent phenol; Benadex® ointment, 1 percent phenol; Kip for Burns® ointment, 0.5 percent phenol; Noxzema Medicated Cream®, 0.5 percent phenol; Tanurol® ointment, 0.75 percent phenol; Dri Toxen® cream, 1 percent phenol; Peterson's ointment®, 2.5 percent phenol. The quantities of these drugs used are not under control. In addition, some feminine hygiene products and hemorrhoidal products contain phenol (Huff, 1978; Am. Pharm. Assoc. 1977).

PHARMACOKINETICS

Absorption

Phenol is readily absorbed by all routes of entry. Absorption is rapid, as illustrated by the fact that acutely toxic doses of phenol can produce symptoms within minutes of administration, regardless of the route of administration.

As noted earlier in this document, Piotrowski (1971) exposed human volunteers in climate-controlled inhalation chambers to phenol administered through face masks to eliminate the influence of dermal exposure. He found that, initially, an average of 80 percent of the phenol was retained in the lungs. The percentage of retained phenol dropped during the experiment, so that after 6 to 8 hours an average of only 70 percent of the inhaled phenol was retained in the lungs. Subsequently, Piotrowski (1971) exposed his volunteers for 6 to 8 hours to various phenol concentrations in the exposure chamber atmosphere, while permitting them to breathe clean air through the face masks. He found that phenol vapor could be readily absorbed through the intact skin and that normal clothing provided little or no protective effect. He found that the rate of dermal absorption of phenol vapor could be represented by the formula $A=(0.35)C$, where A equals the amount of phenol absorbed in mg/hr, and C is the phenol concentration in mg/m^3.

When the data presented by Ohtsuji and Ikeda (1972) (see Inhalation section) are recalculated utilizing the efficiency of inhalation data and the skin absorption coefficient reported by Piotrowski, the figures presented may be confirmed.

Distribution

Phenol is rapidly distributed to all tissues in animals that have been poisoned with the compound. Within 15 minutes of an oral dose, the highest concentrations are found in the liver, followed by heart, kidneys, lungs, blood, and muscle (Deichmann, 1944) (Table 4). As time progresses, concentrations become fairly uniform and start to decrease as the body begins to clear the phenol;

TABLE 4

Distribution of Phenol in the Organs of Rabbits After an Oral Dose of 0.5 g/kg[a]

Tissue	Phenol	Died after 15 min.	Died after 82 min.	Killed after 2 hrs.	Killed after 2½ hrs.	Killed after 6 hrs.
		Concentration of Phenol in mg/100 g tissue				
Liver	Free	63.7	22.4	3.4	13.5	0.5
	Conjugated	0.9	4.2	3.2	6.0	9.4
	Total**	64.6	26.6	6.6	19.5	9.9
Blood	Free	30.8	22.4	5.8	11.3	6.5
	Conjugated	0.9	5.3	8.0	10.2	9.8
	Total	31.7	27.7	13.8	21.5	16.3
Kidneys	Free	35.3	13.4	4.8	11.2	2.6
	Conjugated	0.8	7.4	22.8	12.9	30.0
	Total	36.1	20.8	27.6	24.1	32.6
Lungs	Free	34.2	20.8	5.4	12.2	1.5
	Conjugated	1.8	4.7	6.7	5.1	3.0
	Total	36.0	25.5	12.1	17.3	4.5
Heart, Thymus, Testes, Spleen	Free	53.0	21.0	6.8	14.0	7.5
	Conjugated	0.6	2.3	5.7	5.1	7.7
	Total	53.6	23.3	12.5	19.1	15.2
Brain & Cord	Free	31.3		6.8	10.4	2.5
	Conjugated	0.5		0.7	0.3	0.4
	Total	31.8		7.5	10.7	2.9
Muscle	Free	19.0	8.2	9.2	12.0	10.1
	Conjugated	0	0.5	1.1	0.8	1.4
	Total	19.0	8.7	10.3	12.8	11.5
Urine	Free		0.5		11.6	11.0
	Conjugated	no sample	14.0	no sample	52.0	12.3
	Total		14.5		63.6	23.3
Exhaled air	Free	0	0.1*	0.7*	0.1*	0.2*
	Conjugated					
	Total	0	0.1	0.7	0.1	0.2

[a]Source: Adapted from Deichmann, 1944.
*Phenol in total air exhaled.
**Total phenol obtained by summation of free and conjugated fractions.

the concentrations of total phenol in the kidney remain relatively constant for the first six hours after oral dosing. In rabbits, roughly 77 percent of the administered dose is excreted in the urine during the first 24 hours, and about 20 percent is completely metabolized. In summary, the distribution of phenol presents a rapid absorption phase, followed by rapid generalized distribution to all organ systems, followed by relatively rapid metabolism and excretion.

The data of Piotrowski (1971) similarly indicate a rapid rate of clearance of phenol in man, even though his study did not provide distributional data for various organs.

Metabolism

Free and conjugated phenol appear to be normal trace constituents of the human body and have also been found in other mammalian species (Harborne, 1964). Values reported for phenol concentrations in normal human blood differ markedly among various investigators. Ruedemann and Deichmann (1953) reported normal blood values to be 1.5 mg/l for free phenol and 3.5 mg/l for conjugated phenol. In a brief list of "normal" human blood values, NIOSH (1976) cites ranges for free phenol of from none or traces to 40 mg/l and lists conjugated phenol concentrations ranging from 1 to 20 mg/l. The variability appears to be due in part to the specificity of the analytical method used to detect phenol (Ikeda and Ohtsuji, 1969) and to the amount of dietary protein which increases urinary phenol excretion (Folin and Denis, 1915). More recent values determined by gas-liquid chromatography are 0.04 to 0.56 mg/l for free phenol, 1.06 to 5.18 mg/l for conjugated phenols

(Dirmikis and Darbre, 1974), and 2 to 18 mg/l for total phenol (Van Haaften and Sie, 1965).

The urinary excretion of phenol can be increased above background levels by exposure to agents which are normally metabolized to phenol, such as benzene or phenylsalicylate (Kociba, et al. 1976). The urinary excretion levels of phenol in a worker exposed to phenylsalicylate ranged from 150 to 1,371 mg/l. The ingestion of manufacturer's recommended dosages of Pepto-Bismol® (contains phenylsalicylate) resulted in peak urinary phenol levels of 260 mg/l in a human volunteer (Fishbeck, et al. 1975). The normal background concentration for urinary phenol in this series was 1.5 to 5 mg/l, as detected by gas chromatography. After the ingestion of eight doses of Chloraseptic® lozenges at the recommended dosing schedule, the total urinary phenol concentration peaked at 270 mg/l, and the free phenol concentration peaked at 10 mg/l. When dogs were fed 125 mg phenylsalicylate/kg body weight/day for 41 days, the peak urinary phenol concentration was 6,144 mg/l. This treatment was not associated with any reported ill effects (Kociba, et al. 1976).

The metabolism of exogenous phenol has been most clearly presented by Deichmann and Keplinger (1963) for a lethal oral dose of 0.5 g/kg body weight in rabbits and for a sublethal oral dose of 0.3 g/kg body weight in rabbits. These studies are summarized in Figures 1 and 2.

There are some species differences in the metabolism of phenol. Capel, et al. (1972) reported that man, rat, mouse, jerboa, gerbil, hamster, lemming, and guinea pig excreted four major

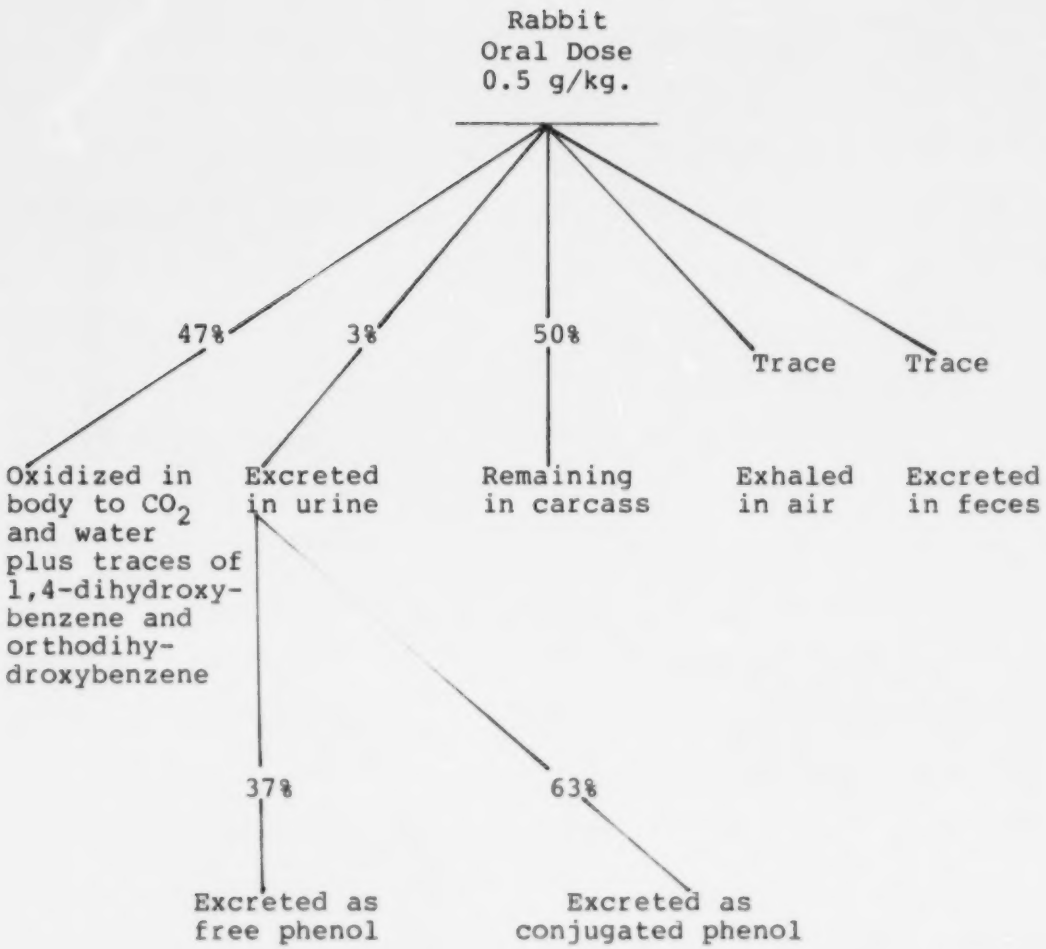

FIGURE 1

Fate of a Lethal Oral Dose of Phenol Analyzed Over 5 Hours

Source: Deichmann and Keplinger, 1963

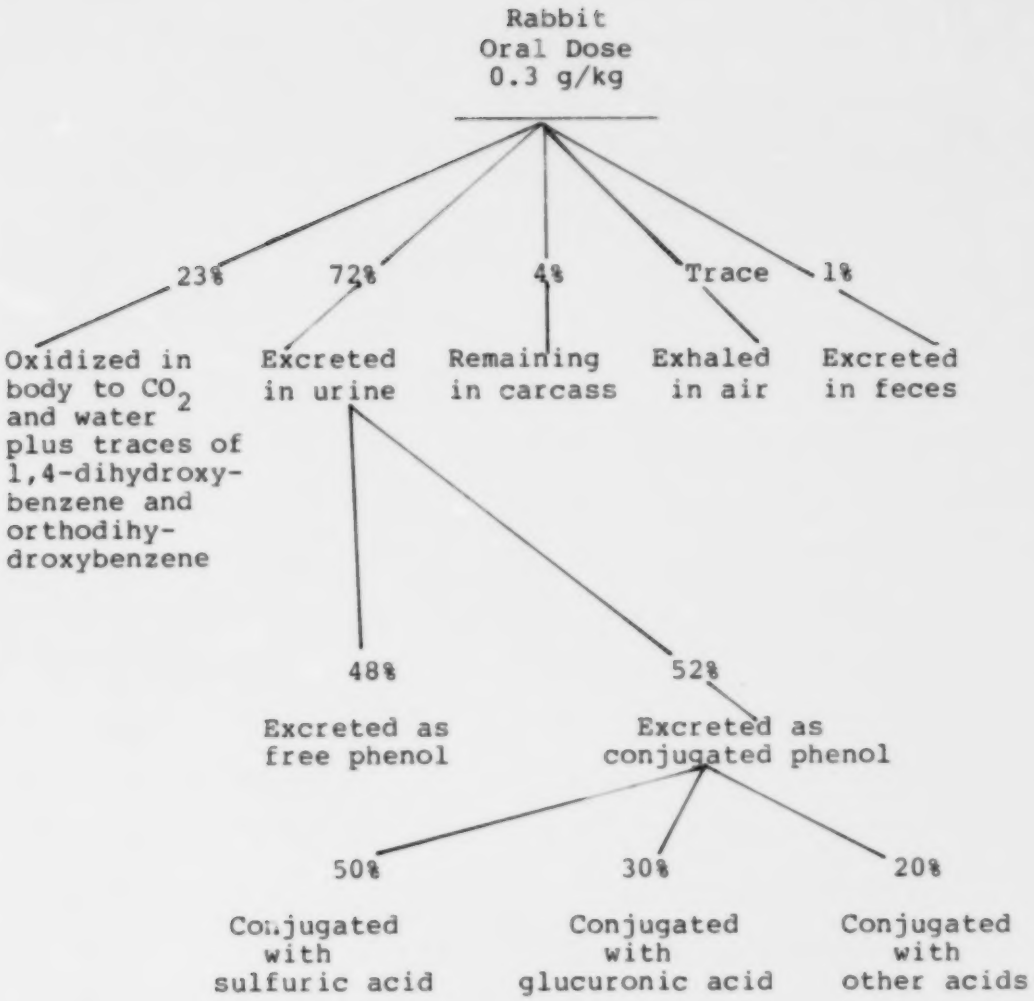

FIGURE 2

Fate of a Sublethal Oral Dose of Phenol Analyzed over 24 Hours

Source: Deichmann and Keplinger, 1963

metabolites: sulfate and glucuronic acid conjugates of phenol and of 1,4-dihydroxybenzene. The squirrel monkey and the capuchin monkey excreted phenyl glucuronide, 1,4-dihydroxybenzene glucuronide, and phenyl sulphate. The ferret, dog, hedgehog, and rabbit excreted phenyl sulfate, 1,4-dihydroxybenzene sulfate, and phenyl glucuronide. The rhesus monkey, fruit bat, and chicken excreted phenyl sulfate and phenyl glucuronide but not 1,4-dihydroxybenzene conjugates. The cat appeared to excrete only phenyl sulfate and 1,4-dihydroxybenzene sulfate, and the pig was found to excrete phenylglucuronide as its major metabolite of phenol. The doses used in this study were relatively low. Miller, et al. (1976) demonstrated that the cat was sensitive to phenol; in addition to sulfate conjugates, free 1,4-dihydroxybenzene was found to be a major metabolite, possibly accounting for the toxicity observed in the cat. The authors also noted that the metabolic pattern was dose dependent. Oehme and Davis (1970) found that with the exception of cats, the rate of phenylglucuronide excretion increased progressively with the dose, so that at high doses phenylglucuronide formation predominated over phenyl sulfate formation.

In man, the rate of absorption, metabolism, and excretion of phenol is relatively rapid. Pietrowski (1971) noted that absorbed phenol was almost completely metabolized and excreted within 24 hours in inhalation experiments near the TLV.

Excretion

In man and all mammals that have been tested, nearly all of the phenol and its metabolites are excreted in the urine. Only minor amounts are excreted in air and in the feces (Deichmann and

Keplinger, 1963). Piotrowski (1971) studied the excretion of phenol in human volunteers who had been exposed to phenol through inhalation or skin absorption. He found that the human body behaved almost like a single compartment with respect to phenol absorption and clearance, with an excretion rate constant of K=0.2 hr^{-1}. This corresponds to a half-life of approximately 3.5 hours (Figures 3 and 4). The half-life is defined as

$$t_{\frac{1}{2}} = \frac{0.693}{K} .$$

Twenty-four hours after administering 300 mg phenol/kg body weight orally to rabbits, Deichmann (1944) reported finding less than 1 percent of the administered dose in the feces.

EFFECTS

Acute, Subacute, and Chronic Toxicity

Regardless of the route of administration, the signs and/or symptoms of acute toxicity in man and experimental animals are similar. The predominant acute action of a toxic dose in man appears to be on the central nervous system, leading to sudden collapse and unconsciousness. In some mammalian species, these effects are preceeded by muscular twitchings and severe convulsions. Mukhitov (as cited in the 1976 NIOSH Criteria Document on Phenol) reported that three humans experienced an increased sensitivity to light after six 5-minute exposures to vapor containing 0.0155 mg phenol/m^3. Four additional subjects responded through the formation of conditioned cortical reflexes after 15-second exposures to 0.024 mg/m^3, and 3 out of 4 subjects responded after 15-second exposures to 0.0155 mg/m^3. The significance of these findings is questionable and unknown.

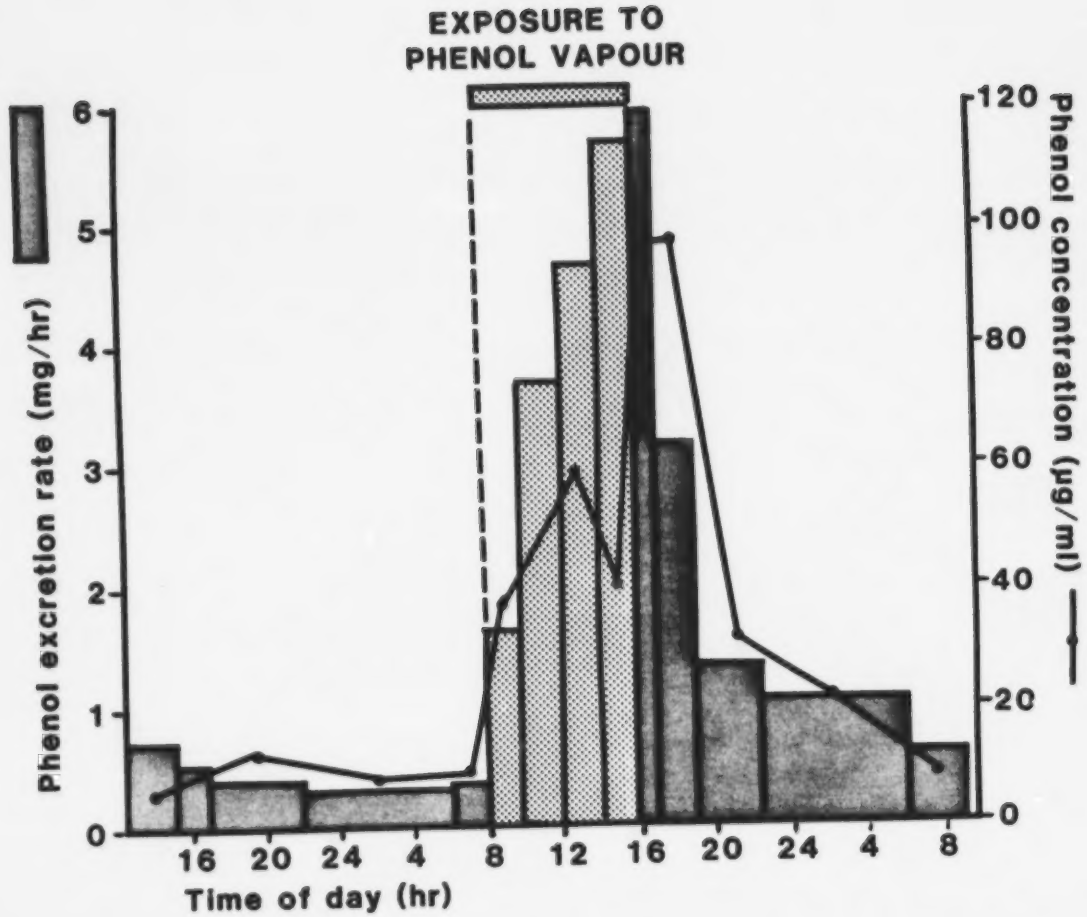

FIGURE 3

Concentrations and excretion rates of phenol in urine in a subject exposed to phenol vapor in a concentration of 18.3 mg/m^3 by inhalation.

Source: Piotrowski, 1971

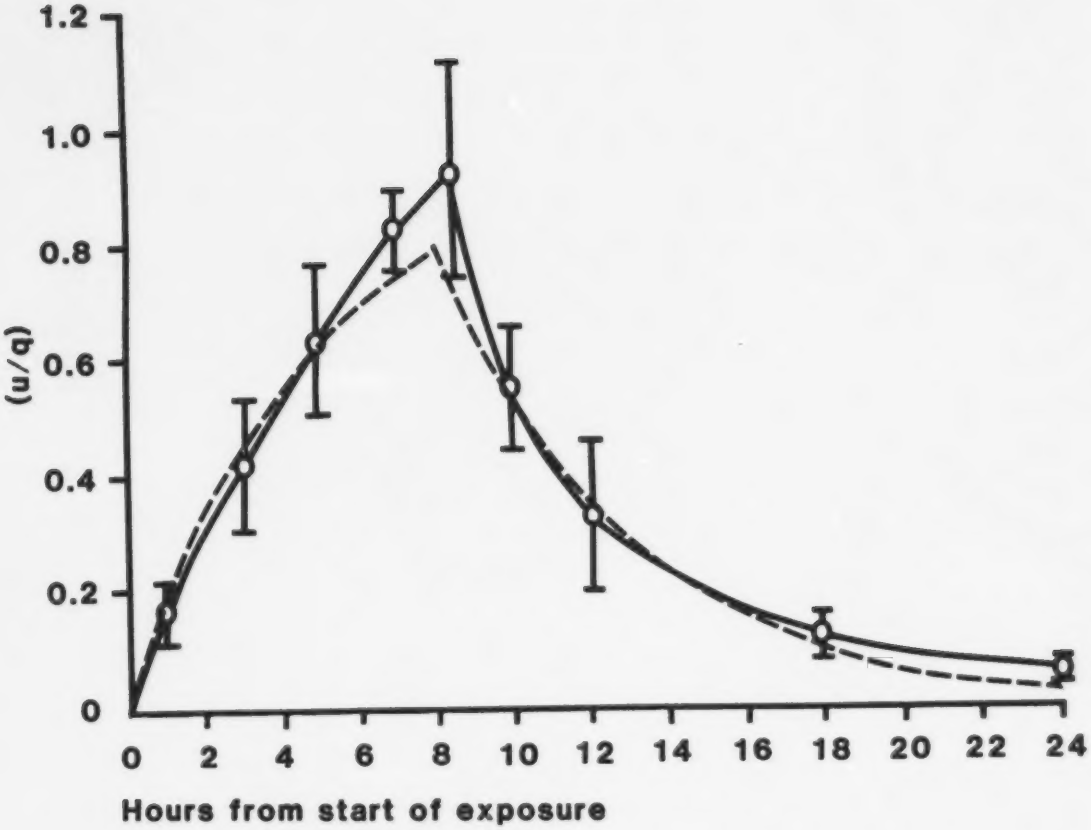

FIGURE 4

Excretion Rate of "Excess" Phenol in Relation to Absorption. Means ± S.D. Dotted Line - Theoretical Curve for K=0.2 $Hour^{-1}$.
Source: Piotrowski, 1971

After the absorption of an acutely toxic dose, the heart rate first increases and then becomes slow and irregular. After an initial rise, the blood pressure falls significantly. Salivation may be evident. There is usually a slight fall in body temperature, and a marked depression in respiration occurs. Death may occur within minutes of the acute exposure and is usually due to respiratory arrest (Deichmann and Keplinger, 1963; Sollmann, 1957). The approximate lethal doses (LD_{50}) for phenol in various species exposed by several different routes are listed in Table 5. It can be noted that most of the data fall within one order of magnitude. The cat appears to be the most sensitive species, which seems to be a consequence of its metabolism of phenol. It is difficult to estimate the LD_{50} for oral exposure to phenol for man, even though phenol has a long history of use in suicidal attempts. A series of human data is presented in Table 6. Dosages were calculated assuming a bodyweight of 70 kg.

When the data in Tables 5 and 6 are compared, it becomes evident that man is not unusually sensitive to the acute effects of phenol when compared to other mammalian species.

Deichmann and Keplinger (1963) describe the following pathological changes associated with acute exposures to phenol:

> The pathological changes produced by phenol in animals vary with the route of absorption, vehicle employed, concentration, and duration of exposure. Local damages to the skin include eczema, inflammation, discoloration, papillomas, necrosis, sloughing, and gangrene. Following oral ingestion, the mucous membranes of the throat and esophagus may show swelling, corrosions, and necroses, with hemorrhage and serious infiltration of the surrounding areas. In a severe intoxication, the lungs may show hyperemia, infarcts, bronchopneumonia, purulent bronchitis, and hyperplasia of the peribronchial tissues. There can be myocardial degeneration and necrosis.

TABLE 5

The Acute Toxicity of Phenol[a] to Nonhuman Mammals

Species	Route	LD_{50} (g/kg)	Reference
Cat	Subcut.	0.09	Tollens, 1905
Cat	Oral	0.1	Macht, 1915
Dog	Oral	0.5	Macht, 1915
Guinea Pig	Subcut.	0.68	Duplay & Cazin, 1891
Mouse	Subcut.	0.3	Tollens, 1905
Rabbit	I.V.	0.18	Deichmann & Witherup, 1944
Rabbit	Subcut.	0.5-0.6	Tauber, 1895; Tollens, 1905
Rabbit	Oral	0.6	Clarke & Brown, 1906
Rabbit	Oral	0.4-0.6	Deichmann & Witherup, 1944
Rabbit	I.P.	0.5-0.6	Deichmann & Witherup, 1944
Rat	Subcut.	0.45	Deichmann & Witherup, 1944
Rat	Oral	0.53	Deichmann & Witherup, 1944
Rat	Oral	0.34 (20% emuls.)	Deichmann & Witherup, 1944
Rat	I.P.	0.25 (In olive oil)	Farquharson, et al. 1958
Rat	Dermal	2.5	Deichmann & Witherup, 1944
Rat	Dermal	0.67	Conning & Hayes, 1970

[a]In dilute aqueous solution, unless noted otherwise.

TABLE 6

Oral Toxicity of Phenol in Humans

Total Dose (g)	Estimated* (g/kg)	Effect	Reference
5	0.07	Survived	Willhard, 1886
10-20	0.14-0.29	Died	Stajduhar-Caric, 1968
15	0.21	Survived	Model, 1889
15	0.21	Died	Kronlein, 1873
25-30	0.36-0.43	Died	Geill, 1888
50	0.71	Survived	Geill, 1888
53	0.75	Survived	Bennett, et al. 1950

*assuming a 70 kg bodyweight.

> The hepatic cells may be enlarged, pale, and coarsely granular with swollen, fragmented, and pyknotic nuclei. Prolonged administration of phenol may cause parenchymatous nephritis, hyperemia of the glomerular and cortical regions, cloudy swelling, edema of the convoluted tubules, and degenerative changes of the glomeruli. Blood cells become hyaline, vacuolated, or filled with granules. Muscle fibers show marked striation.

In addition to the above-mentioned effects, the urine is usually dark or "smoky" in appearance, probably due to oxidation products of phenol. The urine may darken further upon standing (Sollmann, 1957).

The symptoms reported by humans who had consumed phenol-contaminated groundwater for approximately one month (Baker, et al. 1978) are summarized in Table 7. The daily dose of phenol consumed was estimated to be 10 to 240 mg.

Deichmann and Oesper (1940) administered phenol to rats in their drinking water for 12 months at 0, 800, 1,200, 1,600, 2,000, and 2,400 mg/l concentrations. This corresponded to an average daily intake of 0, 21, 30, 49, 56, and 55 mg, respectively, of phenol per rat based on actual water consumption data. At the end of the experiment, there were no significant differences in tissue phenol levels between the control and experimental rats. The weight gain of the rats at the two highest dose levels was depressed. A daily oral dose of 56 mg/rat is approximately 30 percent of the single oral dose required to kill a large proportion of rats in a short time. An additional indication of the rapid metabolism of phenol is the fact that the rats that ingested the

TABLE 7

Symptom Distribution of Cases and Controls After Ingestion of Well Water Contaminated by Phenol*

Symptom	Percentage of Individuals	
	Study Group (N = 39)	Control Group (N = 119)
Vomiting	15.4	13.9
Diarrhea	41.0**	13.5
Headache	23.1	16.1
Skin rash	35.9	22.6
Mouth sores	48.7**	12.6
Paresthesia or numbness	13.2	8.4
Abdominal pain	23.1	11.8
Dizziness	21.1	9.3
Dark urine	17.9	3.4
Burning with urination+	10.3	10.0
Fever+	15.4	10.9
Back pain	20.5	11.0
Burning mouth	23.1**	6.8
Shortness of breath	10.3	6.7

*Source: Baker, et al. 1978.
**Significantly greater than controls, $P < .01$, Fisher Exact test.
+Not associated with phenol exposure in previous medical reports.

highest daily amount administered in this test consumed, over a 1-year period, the equivalence of approximately 120 LD_{50} oral doses.

Heller and Pursell (1938) fed phenol to rats in their drinking water over several generations. The results of their experiment are listed in Table 8.

In an unpublished study by Dow Chemical Company (1976), rats were fed by gavage 20 daily doses of 0.1 g phenol/kg body weight. These rats showed slight liver and kidney effects, while rats which received 20 daily doses of 0.05 or 0.01 g phenol/kg body weight demonstrated none of those effects. In a subsequent series of tests, rats received 135 doses of 0.1 or 0.05 g phenol/kg body weight by gavage over a 6-month period. The growth of the rats receiving the phenol was comparable to that of the controls. Very slight liver changes and slight to moderate kidney damage were seen in the rats which had received 0.1 g phenol/kg. The feeding of 0.05 g phenol/kg resulted only in slight kidney damage.

In a 41-day feeding study, Kociba, et al. (1976) fed 125 mg phenylsalicylate/kg/day to beagle dogs. Since phenylsalicylate is metabolized to phenol, this resulted in urinary phenol levels up to 6,144 mg/l. This high level of phenol excretion was not associated with any discernible ill effects in the dogs. Repeated exposures to phenol at high concentrations have resulted in chronic liver damage in man (Merliss, 1972).

TABLE 8

The Effect of Phenol Solutions Upon Rats*

Phenol Drinking Solutions mg/l	Growth	Reproduction	Comments
100	Normal	5 generations	Splendid condition
500	Normal	5 generations	Appearance good
1,000	Normal	5 generations	Food & water intake satisfactory
3,000	Normal	3 generations	General appearance good
5,000	Normal	3 generations	General appearance good
7,000	Below normal	2 generations	Stunted growth in young
8,000	Fair	2 generations	Many young died
10,000	Retarded	Retarded	Young not cared for
12,000	Retarded	None	Old died in hot weather

*Source: Heller and Pursell, 1938

Synergism and/or Antagonism

No significant evidence could be found to support the occurrence of synergistic or antagonistic actions of phenol with other compounds in mammals.

Challis (1973) reported that phenol could react rapidly with nitrites *in vitro* to produce p-nitrosophenol.

Teratogenicity

The work by Heller and Pursell (1938), which has been discussed previously, demonstrated no significant effects of phenol on reproduction in rats receiving 100 to 5,000 mg phenol/l in their drinking water over 3 to 5 generations. This study, however, was not designed specifically as a teratogenicity study.

Mutagenicity

Demerec, et al. (1951) reported that phenol produced back-mutations in *E. coli* ranging from streptomycin dependence to non-dependence. Significant back-mutations occurred at 0.1 to 0.2 percent phenol concentrations. However, at these concentrations the survival of bacteria was only 0.5 to 1.7 percent. Dickey, et al. (1949) found phenol to be nonmutagenic in *Neurospora*. Hadorn and Niggli (1946) found phenol mutagenic in *Drosophila* after exposing the gonads of *Drosophila* to phenol *in vitro*.

The existing information on the mutagenicity of phenol is equivocal and needs to be re-examined through the use of better established methodologies.

Carcinogenicity

Boutwell and Bosch (1959) tested the tumor promoting activity of phenolic compounds in various strains of mice. Mice that had

been exposed to a single dose of the initiator 9,10-dimethyl-1,2-benzanthracene (DMBA) by skin painting were given repeated dermal applications of selected phenols. In one experiment in this series, following initiation with DMBA and promotion by croton oil through skin painting, mice which had been specially inbred for sensitivity to develop tumors received a single application of 75 μg DMBA to the shaved skin. This was followed one week later by twice-weekly dermal applications of 2.5 mg phenol (as a 10 percent solution in benzene) for 42 consecutive weeks. The mice receiving this dosage of phenol exhibited severe skin damage, decreased body weight, and increased mortality. After 13 weeks, 22 out of 23 mice had developed papillomas, and 73 percent had developed carcinomas. In a group of mice which were treated with DMBA only, 3 out of 21 survivors exhibited papillomas after 42 weeks. In a group exposed to twice-weekly skin paintings with 10 percent phenol alone, 5 out of 14 survivors (36 percent) had papillomas after 52 weeks. The skin painting with phenol was continued until the 72nd week, at which time one fibrosarcoma was diagnosed. Other strains of mice (Holtzman, CAF_1, and C3H) also produced papillomas after initiation with DMBA and subsequent skin painting with 10 percent phenol, but the incidence was lower. The same schedule of application of 1.25 mg phenol twice-weekly to Rusch's special breed of Sutter mice resulted in a lower incidence of papillomas and carcinomas. No carcimomas occurred in the standard breeds of mice when exposed to phenol without pretreatment with DMBA. Tests with a 20 percent phenol solution (5 mg/mouse) caused a number of deaths due to systemic toxicity.

Salaman and Glendenning (1957) reported that "S" strain albino mice showed strong promoting activity for tumor formation after initiation with 0.3 mg DMBA followed by repeated skin applications of 20 percent phenol. Twenty percent phenol solutions produced significant damage to the skin and were weakly carcinogenic when applied alone. Phenol in a 5 percent solution had a moderate promoting effect, but was not carcinogenic without previous initiation.

Van Duuren, et al. (1971) found phenol (3 mg/mouse, 3 x/week) to have only slight promoting activity in ICR/Ha Swiss mice after initiation with benzo(a)pyrene (BaP). In subsequent experiments, Van Duuren, et al. (1973) demonstrated that phenol is not cocarcinogenic since, when it is repeatedly applied together with BaP, tumorigenesis is inhibited slightly. This partial inhibitory effect in cocarcinogenesis experiments was subsequently confirmed by Van Duuren and Goldschmidt (1976).

In conclusion, phenol appears to have tumor-promoting activity in many strains of mice when repeatedly applied to the shaved skin after initiation with known carcinogens. The tumor-promoting activity is highest at dose levels of phenol which have some sclerosing activity, but also occurs in sensitive strains at phenol concentrations which do not produce obvious skin damage. Phenol has no cocarcinogenic activity when repeatedly applied simultaneously with BaP to mouse skin, but it reduces the incidence of tumor formation slightly. When applied repeatedly to the skin of a specially bred strain of Sutter mice, phenol exhibits carcinogenic activity, especially at concentrations which produce repeated skin dam-

age. Phenol has not been found to be carcinogenic when applied alone to the skin of standard strains of mice.

While the existing qualitative data derived from skin painting in one sensitive strain of mice provide suspicion for a weak carcinogenic response to phenol, the protocol was found, in agreement with NIOSH (1976), to be inappropriate and inadequate for the purpose of judging phenol to be a carcinogen in ingested water.

CRITERION FORMULATION

Existing Guidelines and Standards

In 1974, the Federal standard for phenol in air in the workplace was 19 mg/m^3 or 5 ppm as a time-weighted average (39 FR 125). This coincided with the recommendation of the American Conference of Governmental Industrial Hygienists (1977). The NIOSH (1976) criterion for a recommended standard for occupational exposure to phenol is 20 mg/m^3 in air as a time-weighted average (TWA) for up to a 10-hour work day and a 40-hour work week, with a ceiling concentration of 60 mg/m^3 for any 15-minute period.

The U.S. EPA interim drinking water limit for phenol is 0.001 mg/l, which is largely an aesthetic standard based on the objectionable taste and odor produced by chlorinated phenols; this limit is identical to the 1962 U.S. PHS Drinking Water Standard. In response to a phenol spill in southern Wisconsin, the U.S. EPA proposed on November 26, 1974 a local emergency standard of 0.1 mg phenol/l as being temporarily acceptable for human consumption (Baker, et al. 1978).

Current Levels of Exposure

The National Organic Monitoring Survey (U.S. EPA, 1977) reported finding unspecified concentrations of phenol in 2 out of 110 raw water supplies. The survey found no phenol in any finished water supplies. The National Commission on Water Quality (1975) reported that the annual mean phenol concentration in the lower Mississippi River was 1.5 µg/l in 1973, with a maximum of 6.7 µg/l. Endogenously produced phenols in man occur at significantly higher concentration than this.

Occupational exposures at a threshold limit value (TLV) of 20 mg/m^3 TWA would result in the absorption of 105 mg phenol from the inspired air, assuming moderate to low activity (7 m^3 air breathed per eight hours) and an absorption efficiency of 75 percent. During heavier activity (equivalent to 20 m^3 inspired in eight hours), the absorption would rise to 300 mg phenol for an 8-hour shift. The additional skin absorption would be expected to substantially increase these quantities.

Special Groups at Risk

In 1976, NIOSH estimated the number of people who may be exposed to phenol to be 10,000. This reflects the number of people who are employed in the production of phenol, its formulation into products, or the distribution of concentrated phenol products. In addition, an uncertain but probably large number of people will have intermittent contact with phenol as components of medications or in the workplace as chemists, pharmacists, biomedical personnel, and other occupations.

Basis and Derivation of Criterion

Heller and Pursell (1938) reported no significant effects in a multi-generation feeding study in rats at 100, 500, and 1,000 mg phenol/l of drinking water for five generations and at 3,000 and 5,000 mg/l for three generations. Assuming a daily water intake of 30 ml and an average body weight of 300 grams, these rats would have received doses of 10, 50, 100, 300, and 500 mg/kg/day. The upper range approaches a single LD_{50} dose per day. Deichmann and Oesper (1940) reported no significant effects in rats receiving 21, 30, 49, 56, and 55 mg/day in their drinking water for 12 months.

However, neither of these studies reported detailed pathological or biochemical studies, but relied mainly on the weights and general appearance of the animals for evaluation. In a more recent study (Dow Chem. Co., 1976), 135 dosings by gavage over six months at 100 mg phenol/kg/dose resulted in some liver and kidney damage. At 50 mg/kg/dose, however, the exposure resulted in only slight kidney damage. It must be borne in mind that in the first two studies the phenol was incorporated into the drinking water, so that the daily dose was taken gradually. In the Dow study, the phenol was administered in a single slug. A 500-fold uncertainty factor applied to the 50 mg/kg exposure in the Dow study would provide an estimated acceptable level of 0.1 mg/kg/day for man.

The 500-fold uncertainty factor was selected for a number of reasons. In the case of phenol, a great deal of information on human exposure exists. Long-term animal data are available as well; however, the detail in these studies is very incomplete. Shorter-term studies of sufficient detail provide the lowest dose level in animal studies for which an adverse effect was seen. It was judged that the existing data did not fully satisfy the requirements for the use of a 100X uncertainty factor, but were better than the requirements for a 1,000X uncertainty factor [National Academy of Sciences (NAS), 1977]. Consequently, an intermediate 500X uncertainty factor was selected.

When one examines through use of the Stokinger and Woodward model (1958) the amount of phenol absorbed through inhalation near the TLV of 20 mg/m^3 for occupational exposures, one finds that with a breathing rate of 10 m^3/8-hour day and 75 percent absorption, a

70 kg man would absorb approximately 2.14 mg/kg body weight/working day, assuming no skin absorption. The use of the Stokinger-Woodward model may be applicable to estimate acceptable intake from water.

It has been established that phenol is absorbed rapidly by all routes and is subsequently rapidly distributed. If a 10-fold safety factor is applied to the projected doses absorbed from inhalation at the TLV (which already incorporates some safety factors), then the projected acceptable level would be 0.2 mg/kg/day. The estimate from animal data is 0.1 mg/kg/day. On the basis of chronic toxicity data in animals and man, an estimated acceptable daily intake for phenol in man should be 0.1 mg/kg/day or 7.0 mg/man, assuming a 70 kg body weight. Therefore, assuming 100 percent gastrointestinal absorption of phenol, the consumption of 2 liters of water daily and 6.5 g of contaminated fish having a bioconcentration factor of 1.4 would result in a maximum permissible concentration of 3.5 mg/l for the ingested water.

The equation for calculating the criterion for the phenol content of water given an Acceptable Daily Intake (ADI) is

$$2X + (0.0065)\ (BCF)\ (X) = ADI$$

where

2 = amount of drinking water, l/day

X = phenol concentration in water, mg/l

0.0065 = amount of fish consumed, kg/day

BCF = bioconcentration factor, mg phenol/kg fish per mg phenol/l water

ADI = limit on daily exposure for a 70 kg person

$2X + (0.0065)\ (1.4)X = 7.0$ mg/day

$X = 3.5$ mg/l

This water quality criterion is in the range of reported taste and odor threshold values for phenol listed in Table 2. It must be noted that this value has been derived for unchlorinated phenol.

It is recognized that when ambient water containing this concentration of phenol is chlorinated, various chlorinated phenols may be produced in sufficient quantities to produce objectional taste and odors (see Introduction). Therefore, while the criterion for ambient water is 3.5 mg phenol/l, the possible consequences of chlorination treatment of such water may have to be considered for specific local conditions. In those cases where significant chlorination of ambient water is practiced, reference is made to the water quality criteria for 2-chlorophenol (U.S. EPA, 1980b) and 2,4-dichlorophenol (U.S. EPA, 1980c).

In summary, based on the use of chronic toxicologic test data for rats and an uncertainty factor of 500, the criterion for phenol corresponding to the calculated acceptable daily intake of 0.1 mg/kg is 3.5 mg/l. Drinking water contributes $>$ 99 percent of the assumed exposure, while eating contaminated fish products accounts for $<$ 1 percent. The criterion level could alternatively be expressed as 769 mg/l if exposure is assumed to be from the consumption of fish and shellfish products alone.

Since the odor and taste detection threshold concentrations for phenol are well below the toxicity-based criterion level derived above, the ambient water quality criterion is based on organoleptic data. It should be emphasized that this criterion is based on aesthetic quality rather than health effects. However, to the extent that this criterion is derived from the chronic toxicity

study of Dow Chemical Co. (1976), it is also likely to be protective of human health.

The data of Hoak (1957); Burttschell, et al. (1959); and Dietz and Traud (1978) all indicate that low mg concentrations of phenols in water are capable of producing a discernable odor. Burttschell, et al. (1959) and Dietz and Traud (1978) further observed a distinct flavor alteration of water at low and sub-mg levels, respectively, of this chemical. Although 9 of 21 tasters in the Campbell, et al. (1958) study detected the presence of phenols in water at 14 mg/l (the lowest tested concentration reported), a taste threshold of 60 mg/l was determined based on the methodology of the experiment. The data from these studies, in particular the Burttschell, et al. (1959) and Dietz and Traud (1978) experiments, are considered to be reasonably mutually supportive [i.e., Hoak (1957), 10 mg/l for odor; Burttschell, et al. (1959), $>$1.0 mg/l for odor and taste; and Dietz and Traud (1978), 4 mg/l for odor and 0.3 mg/l for taste].

Therefore, based on the prevention of undesirable organoleptic qualities, the criterion level for phenol in water is 0.3 mg/l. This level should be low enough to prevent objectionable organoleptic characteristics for most people and still below animal no-effect concentrations determined in laboratory animals. As more substantive and reliable data become available in the future, a criterion level based on human health effects may be more confidently postulated.

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